Section II (Remarks)

A. Summary of Amendment to the Claims

By the present Amendment, claims 1, 4, 5 and 8 have been amended and new claims 14 and 15 have been added. Claims 3 and 6 were previously cancelled. No new matter within the meaning of 35 U.S.C. §132(a) has been introduced by the foregoing amendments.

Specifically, the amendments to claims 1, 4, 5, and 8 are discussed in detail below. New claims 14 and 15 are supported by claims 1-13, as originally filed and the example on page 7 of the application. The amendments made herein are fully consistent with and supported by the originally-filed disclosure of this application.

Thus, upon entry of the amendments, claims 1, 2, 4, 5, and 7-15 will be pending, of which claims 9-13 are withdrawn from consideration.

B. Claim Objections

In the Office Action mailed October 25, 2010, claim 1 was objected to for inclusion of acronyms PHA and PWM which were not spelled out in the first instance. As amended, the full-length terms for the acronyms are included in claim 1 with the acronyms in parentheses. Support for such amendments is found in the specification at page 7, lines 31-32. The examiner stated that "[i]t would be remedial to amend the claim to define the acronym…" As such, the amendment of the claim has overcome the objection. Withdrawal of the objection is respectfully requested.

Also in the Office Action mailed October 25, 2010, claims 2 and 13 were objected to for containing improper status identifiers in the Response submitted November 15, 2009. As submitted herewith, the status identifiers properly identify claim 2 as "Previously Presented" and claims 13 as "Withdrawn." Withdrawal of the objection is respectfully requested.

Further, claim 8 has been objected as being of improperly dependent form from claim 1. By the present response claim 8 has been amended to clarify that the stimulation index is determined "…in step (e)..." Claim 1 has been amended to clarify the calculation of the stimulation index recited in claim 1(e). The amendment to claim 1 is supported in the specification in the

paragraph spanning pages 5-6. As amended, claim 8 further limits the calculation recited in claim 1. Withdrawal of the objection is respectfully requested.

C. Rejection of the Claims Under 35 U.S.C. §112 – Indefiniteness

In the Office Action mailed October 25, 2010, the examiner has rejected claims 1, 2, 4, 5, 7 and 8 under 35 U.S.C. §112, second paragraph as indefinite. In response, applicants provide the following comments.

The examiner's attention is respectfully directed to Section I above, where claim 1 has been amended in relevant part as follows:

the language "or an early stage of or a predisposition for this disease" has been deleted from the preamble of claim 1;

the phrase "a patient sample comprising lymphocytes" in part (a) of claim 1 has been amended to recite "a sample from a patient, wherein the sample comprises a cell population comprising lymphocytes" in accordance with the examiner's suggestion;

the phrase "quotient of the number of lymphocytes bearing CD69 in step (b) and step (d)" in part (e) of claim 1 has been amended to recite "quotient of the number of lymphocytes bearing CD69 by dividing the number obtained from step (d) by the number obtained from step (b)" in order to clarify that the quotient is calculated by dividing the number obtained from step (d) of claim 1 by the number obtained from step (b) of claim 1; and

step (f) of claim 1 has been further amended to clarify the relationship between the calculated stimulation index and the "method of diagnosing Alzheimer's disease" recited in the preamble. Specifically, "detecting" has been substituted with "determining" and a recitation that a sample with an index of less than 10 is not from a patient suffering from Alzheimer's disease, in order to demonstrate a diagnosis step, as requested by the examiner.

Claim 4 has been amended to depend from pending claim 1 and is therefore no longer dependent from a cancelled claim.

Claims 4 and 5 have been amended to clarify that these method steps further limit the method of claim 1, in accordance with the examiner's suggestions at page 5 of the Office Action.

Claims 2, 7 and 8 were rejected by the examiner as indefinite for depending from indefinite claims. Each of claims 2, 7 and 8 depend from claim 1, which, as amended, is in compliance with the requirements of 35 U.S.C. § 112, second paragraph and is definite. Accordingly, in the claims set provided in Section I above, claims 2, 7 and 8 are not dependent upon an indefinite claim. Withdrawal of the rejection is respectfully requested.

The above-described amendments address all indefiniteness bases for rejection, as set forth by the examiner in the Office Action mailed October 25, 2010. Withdrawal of the rejections is therefore respectfully requested.

D. Rejection of the Claims Under 35 U.S.C. §112 – Enablement

In the Office Action mailed October 25, 29010, the examiner maintained the rejection of claims 1, 2, 4, 5, 7 and 8 as failing to comply with the enablement requirement. Applicants respectfully traverse the rejection.

Initially, the examiner's attention is again respectfully drawn to Section I above. By the amendments indicated therein, claim 1 has been amended to recite "[a] method of diagnosing Alzheimer's disease" and the elements "or an early stage of or a predisposition for this disease" have been cancelled from the claim. As such, claim 1 no longer encompasses methods of diagnosing early stages of Alzheimer's disease or a predisposition for Alzheimer's disease. All of claims 2, 4, 5, 7 and 8 depend directly or indirectly from claim 1 and therefore are similarly amended in scope. The rejection is therefore moot with respect to methods of diagnosing early stages of Alzheimer's disease or a predisposition for Alzheimer's disease. Withdrawal of the rejection with regard to these aspects is respectfully requested.

It was the examiner's assertion in the Office Action mailed October 25, 2010 that the claims as pending prior to the amendment presented herein lacked enablement as not supported by the

specification with respect to the diagnosis of Alzheimer's disease with a reasonable expectation of success (Office Action mailed October 25, 2010, p. 6, 2d para.). Furthermore, the examiner maintained that the disclosure as filed is merely speculative (Office Action mailed October 25, 2010, p. 9, last para.).

The Response submitted November 15, 2009 was accompanied by a Declaration under 37 C.F.R. §1.132 by Inventor Thomas Arendt. The examiner concluded that Dr. Arendt's Declaration demonstrates that patients with confirmed Alzheimer's disease had a stimulation index of more than 10, but that the data provide no evidence that the method can successfully predict a predisposition for Alzheimer's disease prior to clinical onset or that the stimulation index is positively correlated with scores for early stage dementia (Office Action mailed October 25, 2010, p. 9, 1st para.). The examiner further noted that the "specific [ICD-10 research criteria] methodology is neither disclosed within the instant application nor required by the method steps." (Office Action mailed October 25, 2010, p. 7, 2nd para.)

Applicants respectfully submit that the ICD-10 research criteria referenced in Dr. Arendt's declaration was described in order to verify and confirm the test results of the claimed method, namely a stimulation index of more than 10. The subjects tested have to be classified into a patients group and a healthy individuals group by an alternative methodology, before showing whether the results according the claimed method are accurate. Dr. Arendt's declaration does not state that the ICD-10 research criteria are required by the claimed method. ICD-10 research criteria were only used as an alternative recognized methodology for classifying the test subjects into patients and healthy individuals in order to verify whether the claimed method provides similar results. The methodology described in Dr. Arendt's declaration confirms that a stimulation index of more than 10 is indicative for Alzheimer's disease.

As part of the rejection for lack of enablement, the examiner stated that "[t]here was nothing of record to suggest that a definitive diagnosis of Alzheimer's disease…could be provided by the method as claimed." (Office Action mailed October 25, 2010, p. 9, 1st para.) Applicants respectfully submit that a conclusive diagnosis of Alzheimer's disease is only possible postmortem. However, Dr. Arendt's declaration shows that the claimed method, as described in the specification as filed, provides diagnostic results which correlate with recognized clinical methods of diagnosing Alzheimer's disease such as Mini-Mental State Examination (MMSE), and thus provide a basis for definitive diagnosis of Alzheimer's disease.

The examiner further cited Kusdra et al., *Immunobiology*, 202:26-33, 2000 as evidence that "many diseases have a prominent inflammatory component and …that $CD69^+$ cells may not contribute directly to AD pathogenesis and may be the result of proinflammatory processes in the brain. Since these patients already have an AD diagnosis, it is difficult to determine whether $CD69^+$ would make a good marker for risk assessment before AD onset." (Office Action mailed October 25, 2010, p. 8, last para.)

Kusdra et al. reports that an increase in CD69 monocytes correlated with an Alzheimer's diagnosis, but expresses doubts whether CD69 would make a good marker for risk assessment before AD onset. This reference does not contradict the claimed method as amended; claim 1 does not recite the diagnosis of an early stage or predisposition. Additionally, Kusdra et al. refers to the $CD69^+$ cells present, while the stimulation index of the claimed method refers to the number of $CD69^+$ cells generated upon additional mitogenic stimulation. As such, the stimulation index of the claimed method is a parameter different from the level of $CD69^+$ cells reported by Kusdra et al.; *i.e.* the determination of Kusdra et al. does not comprise or contemplate steps such as those recited in steps (c) to (e) of claim 1 as amended. Thus, the results of Kusdra et al. do not contradict the method of pending claim 1.

While methods comprising mitogenic stimulation of lymphocytes and quantification of the cells by cell sorting using the CD69 surface marker (Neubert et al., cited by the examiner at page 9 of the Office Action mailed October 25, 2010) including using samples from patients with Alzheimer's disease with respect to potentially diagnostic purposes (Stieler et al., cited by the examiner at page 9 of the Office Action mailed October 25, 2010) were known in the art prior to filing of the present application, the claimed method provides the improvement that a reproducible diagnosis can be made by testing only a single sample and calculating a stimulation index according to the method. Because no comparative samples are necessary, the claimed method can be applied advantageously for quick-testing in a physician's practice.

Amended claim 1 does not recite diagnosis of an early stage or predisposition for Alzheimer's disease. Amended claim 1 recites the mitogenic stimulation of a patient sample (preamble), wherein it is determined whether or not this patient sample is from "a patient suffering from Alzheimer's disease". The specific language regarding the diagnosis of an early stage or predisposition has been cancelled from the claim. Therefore, the amended claims do not encompass the diagnosis of an early stage or predisposition for Alzheimer's disease.

The data provided in Dr. Arendt's declaration confirm that a stimulation index obtained and calculated according to the method described in the originally filed specification reproducibly enables one to distinguish between patients suffering from Alzheimer's disease and healthy individuals. Therefore, the method of claim 1, as amended, is enabled with a reasonable expectation of success. Claims 2, 4, 5, 7 and 8, dependent from claim 1, are similarly enabled.

A determination of enablement under 35 U.S.C. §112, first paragraph is based on an evaluation of whether the disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the relevant art to make and use the claimed invention without "undue experimentation." Applicants assert that the disclosure of the present application is so enabling. Withdrawal of the rejection of claims 1, 2, 4, 5, 7 and 8 as failing to comply with the enablement requirement is respectfully requested.

E. Fee Payable for Added Claims

By the present Amendment, 1 new independent claim and 2 new total claims have been introduced. Addition of the new claims brings the total number of claims to fifteen (15), three (3) of which are independent. As the total number of claims does not exceed 20 and the total number of independent claims does not exceed 3, no additional claims fees are due for such added claims.

CONCLUSION

Based on the foregoing, all of applicants' pending claims 1, 2, 4, 5, and 7, 8, 14 and 15 are patentably distinguished over the art, and in form and condition for allowance. The examiner is requested to favorably consider the foregoing and to responsively issue a Notice of Allowance.

This responds to the October 25, 2010 Office Action in the above-identified application. The time for responding to the October 25, 2010 Office Action without extension was set at three months, or January 25, 2011. Applicants hereby request a two month extension of time under 37 CFR § 1.136 to extend the deadline for response to March 25, 2011. Payment of the extension fee of $245.00 specified in 37 C.F.R. § 1.17(a)(2), as applicable to small entity, is being made by on-line credit card authorization at the time of EFS submission of this Response. Should any

additional fees be required or an overpayment of fees made, please debit or credit our Deposit Account No. 08-3284, as necessary.

If any issues require further resolution, the examiner is requested to contact the undersigned attorneys at (919) 419-9350 to discuss same.

Respectfully submitted,

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